

In a telephone conversation (late February 2002) between the examiner and Michael Sanzo (formerly of Pillsbury Winthrop LLP), it was determined by the applicants that Patent Office had misplaced the amendment duly filed on October 25, 2002, thereby delaying examination. The applicants, pursuant to a request by the examiner, facsimile-transmitted a copy of the October 25, 2001, amendment and response along with the stamped receipt on February 28, 2002.

In view of the foregoing, the applicants request that the examiner acknowledge this error. The applicants also request that the Patent Office acknowledge this delay in examination in view of the term of any patent issuing from the present application.

Rejection Based Upon 35 U.S.C. §103(a)

The examiner maintained the rejection of claims 1 and 3-24 under 35 U.S.C. §103(a) as allegedly being unpatentable over Engel *et al.* and Albano *et al.*, Felberbaum *et al.*, and Garfield in view of Deghenghi, Rabasseda *et al.* and Kent. Reconsideration and allowance of the present application based upon the following remarks are respectfully requested.

The examiner cites SEVEN different and unrelated documents to find the presently claimed invention obvious. Specifically, the examiner alleges Engel *et al.* teaches a method of using an LHRH-antagonist for suppressing premature ovulation in controlled ovarian stimulation and assisted reproductive techniques. Albano *et al.* is cited for its alleged teaching of a method of using cetrorelix in suppression of premature ovulation in controlled ovarian stimulation and assisted reproductive techniques, such as IVF and ICSI. Albano is also noted by the examiner for its alleged teaching that progesterone concentration is significantly lowered due to the administration of cetrorelix. The examiner cites Felberbaum *et al.* for its alleged teaching of the usefulness of LHRH-antagonists in a method of suppression of premature ovulation in controlled ovarian and assisted reproductive

techniques. Felberbaum *et al.* is also noted for allegedly teaching a fall of sex steroids due to the administration of LHRH-antagonists. Garfield is cited by the examiner for its alleged disclosure of the use of progestogen, together with an estrogen and an LHRH-antagonist, during follicular phase in a method of controlling ovarian stimulation and preventing conception. Deghngghi is cited for its alleged teaching of the LHRH-antagonists cetrorelix, teverelix, ganirelix and antide. Rabasseda *et al.* is cited for the alleged teaching that LHRH-antagonists such as cetrorelix, ganirelix, and abarelix are known in the treatment of female infertility. The examiner notes Kent allegedly discloses that the combination of progestogens and estrogen is useful in animal contraception.

It remains the examiner's position that it would have been obvious to a one of skill in the art, at the time the invention was made, to "employ the particular LHRH-antagonist such as teverelix, antide, and abarelix and to optimize their effective amounts to be administered, and to schedule or program the ovarian stimulation therapy on Fridays to Mondays and oocyte pick up and ART on Mondays to Thursdays, to employ the particular estrogen, mestranol, in oral contraceptive preparations along with progestogen". *Yet again*, the applicants traverse the foregoing rejection and submit that the cited documents, either alone or in combination do not render the presently claimed invention unpatentable.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Engel *et al.*, Albano *et al.*, and Felberbaum *et al.*, and Garfield either alone or in combination with each other or in further combination with Deghenghi, Rabasseda *et al.* and Kent fail to teach or suggest the applicants' claimed invention of the program and the novel combination of steps that comprises the claimed invention. Specifically, the cited documents, either alone or in combination, fail to teach or suggest a method of therapeutic management of infertility by programming of controlled ovarian stimulation and assisted reproductive procedures the improvement consisting of (a) suppression of premature ovulation with an LHRH-antagonist in controlled ovarian stimulation and assisted reproductive techniques with multiple follicle and oocyte development; (b) programming the start of controlled ovarian stimulation by the administration to a patient of progestogen only -preparations or, alternatively, combined oral contraceptive preparations; (c) exogenous stimulation of the ovarian follicle growth; (d) ovulation induction with HCG, native LHRH, LHRH-agonists or recombinant LH; and (e) application of assisted reproduction techniques, especially of IVF, ICSI, GIFT, ZIFT or by intrauterine insemination by sperm injection, wherein onset of the patient's menstrual cycle and of controlled ovarian stimulation are programmed in order to perform oocyte pickup and fertilization procedures during Mondays to Fridays. Clearly, the inventive method provides, **for the first time**, the use of an LHRH-antagonist in controlled ovarian stimulation cycles programmed by oral contraceptives. Therefore, because the cited documents neither teach nor suggest the applicants' claimed method (to be performed in the specified manner and order), the applicants' claimed invention simply cannot be rendered obvious by the cited documents. Therefore, the applicants respectfully request that the rejection of claims 1 and 3-24 under 35 U.S.C. §103(a) over the cited documents be withdrawn.

It is interesting to note that the examiner admits that the cited documents fail to disclose the claimed program of ovarian stimulation by the administration of oral

contraceptive preparations or the effective amounts of the LHRH-antagonists to be administered during the method. Therefore, the applicants question how the examiner can seriously maintain the present rejection in the face of such a statement.

In the outstanding official action, the examiner stated since all of the applicants' steps are (allegedly) known, that it would have be obvious for one of ordinary skill in the art to combine the steps to achieve the claimed method. While the foregoing may or may not be true, the applicants submit that the prior never teaches nor suggest the steps in the manner and order of the present invention to provide a method of therapeutic management of infertility by programming of controlled ovarian stimulation and assisted reproductive procedures. Thus, it seems to the applicants that the examiner continues to miss the point of the novel method disclosed herein, in which, for the first time, an LHRH-antagonist is used in controlled ovarian stimulation cycles programmed by oral contraceptives. Further, it is interesting to note that the examiner does not address why it would be obvious to take non-programmed cycle process steps and utilize them in a programmed method. Finally, even if each individual step is individually known, the steps taken together are simply not known for use as a method of therapeutic management of infertility by programming of controlled ovarian stimulation and assisted reproductive procedures.

In view of the fact that the examiner used SEVEN references to find the present claims obvious, the applicants submit that the examiner has used impermissible hindsight to find the present claims obvious. Clearly the examiner has done nothing more that use the applicants' disclosure as a road map in rejecting the presently claimed invention.

Thus, the applicants submit that the examiner has failed to present a *prima facie* case of obviousness and as such respectfully request that the rejection of the claims pursuant to 35 U.S.C. §103(a) be withdrawn.

CONCLUSION

In view of the foregoing, the claims are now believed to be in form for allowance, and such action is hereby solicited. If any point remains in issue which the examiner feels may be best resolved through a personal or telephone interview, the examiner is **strongly urged** to contact the undersigned at the number indicated below.

Respectfully submitted,

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